Seasonal influenza vaccination in China

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Seasonal influenza vaccination in China: Landscape of diverse regional reimbursement policy, and budget impact analysis

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ABSTRACT

Background: To explore the current landscape of seasonal influenza vaccination across China, and estimate the budget of implementing a national "free-at-the-point-of-care" vaccination program for priority populations recommended by the World Health Organization.
Methods: In 2014 and 2016, we conducted a survey across provincial Centers for Disease Control and Prevention to collect information on regional reimbursement policies for influenza vaccination, estimated the national uptake using distributed doses of influenza vaccines, and evaluated the budget using population size and vaccine cost obtained from official websites and literatures.
Results: Regular reimbursement policies for influenza vaccination are available in 61 mutually exclusive regions, comprising 8 provinces, 45 prefectures, and 8 counties, which were reimbursed by the local Government Financial Department or Basic Social Medical Insurance (BSMI). Finance-reimbursed vaccination was offered mainly for the elderly, and school children for free in Beijing, Dongli district in Tianjin, Karamay, Shenzhen and Xinxiang cities. BSMI-reimbursement policies were limited to specific medical insurance beneficiaries with distinct differences in the reimbursement fractions. The average national vaccination coverage was just 1.5–2.2% between 2004 and 2014. A free national vaccination program for priority populations (n = 416 million), would cost government US$ 757 million (95% CI 726–789) annually (uptake rate = 20%).
Conclusions: An increasing number of regional governments have begun to pay, partially or fully, for influenza vaccination for selected groups. However, this small-scale policy approach has failed to increase national uptake. A free, nationwide vaccination program would require a substantial annual investment. A cost-effectiveness analysis is needed to identify the most efficient methods to improve coverage.

1. Introduction

Annual seasonal influenza epidemics represent a major disease burden globally, with 3–5 million cases of severe illness that result in over a quarter of a million deaths every year [1]. Influenza vaccination is the most effective way to prevent disease, and the World Health Organization (WHO) recommends annual seasonal influenza vaccination for pregnant women, children aged six to 59 months, the elderly, persons with specific chronic medical conditions, and health-care workers (hereafter called the "priority populations") [2]. As of 2014, over 100 countries worldwide already have seasonal influenza vaccination policies that recommend vaccination of at least one of the risk groups [3]. Over 40% of countries list seasonal influenza vaccination on their National Immunization Schedule, including most countries across North

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and South America, Europe, and some countries in African, South-East Asia, and the West Pacific Region [4–8].

Despite seasonal influenza being associated with between 67,000 and 430,000 annual excess respiratory and circulatory deaths on average for five pre-pandemic influenza seasons 2004–2005 through 2008–2009 [9], influenza vaccination is not included on the National Immunization Program (NIP) in China. Therefore, there are no national guidelines for alleviating the cost burden on individuals who wish to receive the vaccine, which may contribute to low vaccine uptake of 1·9% for the entire population in China and 4.3% for the urban residents aged above 60 years old in 9 cities, recorded during the 2008–2009 and 2011–2012 influenza season, respectively [10,11]. Thus, vaccine uptake in China falls substantially below the World Health Assembly (WHA) target of 75% in the elderly by 2010 [12], and also below that of other upper-middle income countries such as Brazil where coverage is over 70% in the elderly [6].

In countries where vaccination costs are subsidized by the respective governments, there is higher national vaccine uptake [13,14]. To our knowledge, only a handful of large cities in China currently provide reimbursement for influenza vaccination. For example, since 2007, Beijing has provided free seasonal influenza vaccination to the elderly and school children, and since 2004, Xi'an city in Shaanxi province has provided free vaccination to those covered by Medicare insurance [10]. Unlike NIP vaccines funded by the central government, there is a diverse patchwork of reimbursement policies that exist at the provincial, prefecture and county levels for influenza vaccination.

WHO has called upon China to include more vaccines in NIP, following a recent vaccine scandal with improperly refrigerated of transported vaccines sold nationwide [15]. To inform a future national government-funded free seasonal influenza vaccination program for China that harnesses the advantages of regionally administrated schemes and provides a sustainable public health strategy, we conducted a survey to explore the current landscape of influenza vaccination, including reimbursement policies, eligible subgroup sizes, and influenza vaccine uptake across China. We then estimate the budget needed to implement a nationwide "free-at-the-point-of-care" vaccination program by conducting a budget impact analysis parameterized with province-level data for the size of the subgroups—delineated by age and risk group—eligible to receive an influenza vaccine.

2. Methods

2.1. Landscape of influenza vaccination across China

2.1.1. Regional reimbursement policies for influenza vaccination

Between August and November, 2014, we conducted a survey across all 31 provincial Centers for Disease Control and Prevention (CDCs) to collect information on provincial-level reimbursement policies for influenza vaccination (and at the prefecture- and county-level if applicable), and performed a web search of below official websites to validate the responses: (1) all 31 provincial-level and 333 prefecture-level governments, (2) the Bureau of Human Resources and Social Security, (3) the Commission of Health and Family Planning, and (4) the provincial CDCs (see questionnaire in supplementary 1). Nearly two years have passed since our initial survey mentioned above. To check whether there were major new vaccination policies implemented across China between December 2014 and September 2016, we re-searched all the aforementioned official websites.

2.1.2. Eligible subgroup size of regional reimbursement policies

For the regions where reimbursement policies are available for influenza vaccination, the eligible population mainly include subgroups at a certain age, school children, health-care workers, and/or insured persons of Basic Social Medical Insurance (BSMI) (including New Rural Cooperative Medical Insurance for Rural Residents (NRCMI), Basic Social Medical Insurance for Urban Employees (BSMIUE), and Basic Social Medical Insurance for Urban Residents (BSMIUR)) (see details for the introduction to BSMI in supplementary 2). To estimate the size of subgroups eligible for reimbursement, local age-specific population data and the number of school children were obtained from National Bureau of Statistics [16], the number of health-care workers was gained from local Health Statistics Yearbook, and the number of insured persons was collected from the four official websites described above.

2.1.3. Influenza vaccine coverage

We estimated the national yearly influenza vaccine uptake rate in China using the annual number of doses of seasonal influenza vaccine released between 2004 and 2014 from the website of the National Institutes for Food and Drug Control. In China, all unsold influenza vaccines are returned to the manufacturers at the end of each season for disposal. We used a 14–31% return rate [10], and 1–10% vaccine wastage rate, resulting from physical damage, expiration, losses in transit, consistent with the wastage of single dose vaccines in 7 GAVI-eligible countries [17–19].

2.2. Budget impact analysis under a free national vaccination program for priority populations

2.2.1. The size of priority populations

We used 2013 National Bureau of Statistics age-specific population data to estimate the size of priority populations stratified by provinces [16]. According to the latest guidelines of influenza vaccination issued by China CDC [20], the priority populations for influenza vaccination in China includes those recommended by WHO [2], and family members and caregivers of infants younger than 6 months. For global comparisons, we used the WHO definition of priority populations. The detailed calculation of priority populations size was provided below.

We estimated the number of pregnant women as the sum of number of live births, still births, fetus deaths and abortions. The number of live births was obtained from China Health Statistical Yearbook (CHSY) in 2013 [21]. The number of still birth and fetus deaths were estimated as the product of the number of perinatal deaths [21] and the fraction of those deaths which are still births and fetus deaths (68.59%) [22]. We estimated the number of abortions by dividing the number of induced abortions [21] by the proportion of induced abortions (88.54%) [23]. The number of health-care workers was obtained from the CHSY in 2013 [21]. To minimize the overlap among persons with specific chronic medical conditions, children aged six to 59 months and the elderly, we estimated the number of persons with chronic illness only in those aged 5–59 years, multiplying the age-specific population size by the age-specific prevalence of chronic conditions.

We performed a literature review to obtain the prevalence of underlying medical conditions in China which are related to increased risk of hospitalization and mortality if infected with influenza. We searched articles published in PubMed, Wanfang and CNKI during 2000–2014, with terms including above specific disease as "asthma" and "China", and "prevalence"/"disease burden"/"epidemic"/"epidemiological"/"epidemiology". All identified papers were reviewed, and the most recent national representative studies were included [21–39]. We summed the prevalence of each chronic disease to get the prevalence by diseases (e.g., a person with three chronic diseases was counted three times) (Table 1). To get the prevalence by cases (e.g., a person with more than one chronic diseases was counted only one

time), we multiplied prevalence by diseases with a ratio of prevalence by cases to prevalence by diseases, which was obtained from the 4th National Health Service Survey of China in 2008 [35] (Table 1). We specifically estimated the size of priority populations in regions with reimbursement policies as well, using the same methods for estimating that stratified by provinces described above.

2.2.2. Budget impact analysis

We evaluated the budget necessary for a free-at-the-point-of-care trivalent inactivated influenza vaccine (TIV) program for priority populations. TIV is administered in doses of 0·25 ml for infants 6–35 months, and 0·50 ml for the rest of the population [20]. Considering the very low uptake rate [10] of influenza vaccines in China, we assumed conservatively that children aged 6 months to 8 years will have never received an influenza vaccine and therefore would require two doses in the first year of the program. There is significant uncertainty in the coverage that may be achieved in a potential national free vaccination program. The experience of Beijing showed that the uptake in the elderly increased substantially (1.69% in 1999 vs. 43% in 2010) [40,41] after free influenza vaccination was offered in 2007. It is likely that the uptake in other less dense and development provinces would not increase as quickly as Beijing, the capital of China where residents likely have greater access to health care facilities and there are likely disproportionately more educated persons. We estimated the budget with a conservative base-case uptake rate of 20% [42] and a conservative vaccine wastage rate of 10% [17]. We also conducted a sensitivity analysis to estimate the impact of uncertainty of uptake rate (10%, 40% and 75%), and wastage rate (lower limit = 1%) [17] on the total budget. Moreover, we used age-specific vaccine uptake as well as risk-group-specific vaccine uptake (40% for children aged 6–59 months, 20% for the elderly, persons aged 5–59 years with underlying chronic illness and health-care workers, and 10% for pregnant women, according to the difference in uptake rates which was observed in nine cities in China [11]) to estimate the national budget.

Influenza vaccine types that are used in specific regions are determined and centralized purchased by local provincial, prefecture or even district level CDCs, and then distributed to lower level CDCs and/or Points of Vaccination [43]. Procurement of influenza vaccine is conducted by negotiated between government and manufactures. To obtain the influenza vaccine cost in China, we searched the official websites of provincial and prefecture-level authorities, which included the Price Bureau, Development and Reform Commission, Health Bureau, CDCs and government portal website. When considering the overall vaccination program costs (including training, advocacy, etc.) (US$1.27 per dose for the provincial Expanded Program on Immunization in Guizhou province) [44], and assuming the existing cold-chain infrastructure could be used for a national seasonal influenza vaccination program, the influenza vaccination cost per capita during 2011–2013 was separately US$4.87 per dose (95%CI 4.62–5.11) for 0.25 ml formulation and US$7.17 per dose (95%CI 6.89–7.46) for 0.50 ml formulation. All costs were updated to 2015 CNY using the consumer price index [45] and expressed in US dollars using the median 2015 exchange rate of 1 US$ = 6·2 CNY [46].

3. Results

3.1. Landscape of influenza vaccination across China

3.1.1. Regional reimbursement policies for influenza vaccination

Regular reimbursement policies for influenza vaccination are available in 61 mutually exclusive regions across China, comprising 8 out of 31 provinces, 45 out of other 253 prefectures and 8 out of remaining 1782 counties. Influenza vaccination in these regions was reimbursed fully or partially by the local Government Financial Department (hereafter called Finance-reimbursed vaccination), or BSMI. According to the BSMI types and reimbursement modes, the BSMI-reimbursed policy was further broken down into 3 subgroups: (1) NRCMI-reimbursed vaccination; (2) BSMI-proportional-reimbursed vaccination, which was proportionally reimbursed by BSMIUE and/or BSMIUR; (3) BSMIUE-MSA-reimbursed vaccination which was reimbursed using an individual card of Medical Savings Account (MSA) of BSMIUE.

Annual Finance-reimbursed vaccination is offered free of charge in Beijing, Dongli district in Tianjin, Karamay in Xinjiang province, Shenzhen in Guangdong province and Xinxiang in Henan province. NRCMI-reimbursed vaccination is available in seven counties and one prefecture, BSMI-proportional-reimbursed vaccination available in five prefectures, and BSMIUE-MSA-reimbursed vaccination available in seven provinces and 38 prefectures (there are two types of policies available in Xinxiang and Shenzhen, respectively). There were also several one-off large-scale free influenza vaccination programs in a few cities (e.g., Chengdu of Sichuan province, and Jinzhou of Liaoning province), mainly as a result of natural disasters (e.g., 2008 earthquake in Sichuan province, and 2013 flood in Liaoning province). (Fig. 1 and Table 2, and more details shown in supplementary Table 1s.) It's noted that BSMI-proportional-reimbursed vaccination for insured persons in Xi'an of Shaanxi province was only implemented between 2004 and 2006; in 2015, BSMI resumed reimbursement for influenza vaccination, i.e., urban employees can use the surplus fund of individual BSMIUE MSA card to pay for influenza vaccination for their own and their families.

Significant differences were also observed for the reimbursement fractions among these four reimbursement policies. For example, in BSMI-proportional-reimbursed vaccination regions, the reimbursement fraction ranged from 30% (Zhaoqing in Guangdong province) to 100% (e.g., Kaifeng in Henan province). Importantly, the reimbursement fraction of BSMIUE-MSA-paid vaccination relies on the availability of surplus funds in the individual BSMIUE-MSA accounts (Table 2).

3.1.2. Eligible subgroup size of regional reimbursement policies

The eligibility criteria for reimbursement varied significantly. Annual Finance-reimbursed vaccination was mainly offered for the elderly, school children and health-care workers. BSMI-reimbursement policies were limited to specific medical insurance beneficiaries. Considerable differences were observed for the number of eligible subgroups: Finance-reimbursed vaccination covered 5·7 million persons, NRCMI-reimbursed vaccination covered 7·2 million, BSMI-proportional-reimbursed vaccination covered 5·8 million, and BSMIUE-MSA-reimbursed vaccination covered 102.8 million. The NRCMI-reimbursed vaccination covered over 70% of local population aged 6 months and over. The coverage of most of other reimbursed vaccination was less than 30% (Fig. 2).

In regions with regular reimbursement policies, priority populations represented an average of 31% of the local population aged 6 months and above. In 59% (36/61, excluding Kaifeng and Inner Mongolia where the size of the eligible population was unavailable) of regions, the size of the eligible population was less than that of priority populations (Fig. 2). In 86% (n = 50) of the 58 regions where influenza vaccination was reimbursed by BSMI, the policy focused on the insured persons irrespective of membership in a priority risk group (Table 2). For example, there were 463,000 people in the priority populations in Changji of Xinjiang province, while only 238,300 urban employees registered in BSIMUE were covered by BSMIUE-MSA-reimbursed vaccination.

Table 1
The prevalence of underlying medical conditions related to increased risk of hospitalization and mortality if infected with influenza in China*.

	0-years	5-years	15-years	25-years	35-years	45-years	55-years	60+ years
Chronic obstructive pulmonary disease (COPD) [24,25]	/	/	0.07%	0.45%	1.94%	3.52%	8.05%	15.49%
Asthma [26,27]	2.78%	2.05%	0.37%	0.43%	0.59%	1.07%	1.48%	1.83%
Chronic cardiac disease								
Coronary heart disease [28]	/	/	/	/	0.17%	0.72%	1.30%	1.45%
Chronic heart failure [29]	/	/	/	/	0.40%	1.00%	1.30%	1.30%
Congenital heart disease [30]	/	0.57%	/	/	/	/	/	/
Chronic liver disease								
Primary binary cirrhosis [31]	/	/	0.05%	0.05%	0.05%	0.05%	0.05%	0.05%
Alcoholic liver hepatitis and cirrhosis [32]	/	/	/	1.16%	1.16%	1.16%	1.16%	1.16%
Chronic hepatitis B [33]	/	0.33%	1.17%	1.80%	1.75%	1.46%	1.14%	0.98%
Chronic renal failure [34]	/	/	0.03%	0.03%	0.03%	0.03%	0.03%	0.03%
Chronic haematological disorder [35]	0.06%	0.05%	0.06%	0.11%	0.23%	0.34%	0.34%	0.29%
Chronic neurological disease [35]	0.07%	0.10%	0.21%	0.20%	0.40%	0.48%	0.74%	0.98%
Diabetes [36,37]	/	0.12%	3.98%	5.66%	6.57%	14.17%	17.60%	22.86%
Tuberculosis [38,39]	0.09%	0.09%	0.25%	0.23%	0.29%	0.42%	0.58%	1.11%
Prevalence by diseases (sum of prevalence of above diseases)	3.01%	3.30%	6.14%	10.12%	13.58%	24.41%	33.77%	47.53%
Ratio of prevalence by cases to prevalence by diseases [35]	1.00	1.00	1.00	0.92	0.87	0.82	0.78	0.73
Prevalence by case	3.01%	3.30%	6.14%	9.32%	11.80%	20.09%	26.46%	34.48%

/data were unavailable and assumed to be zero.
* The prevalence of other chronic illness (e.g., immunodeficiencies related to use of immunosuppressive drugs, morbid obesity with a BMI > 40 kg/m^2) were not available, and hence not included in the analysis.

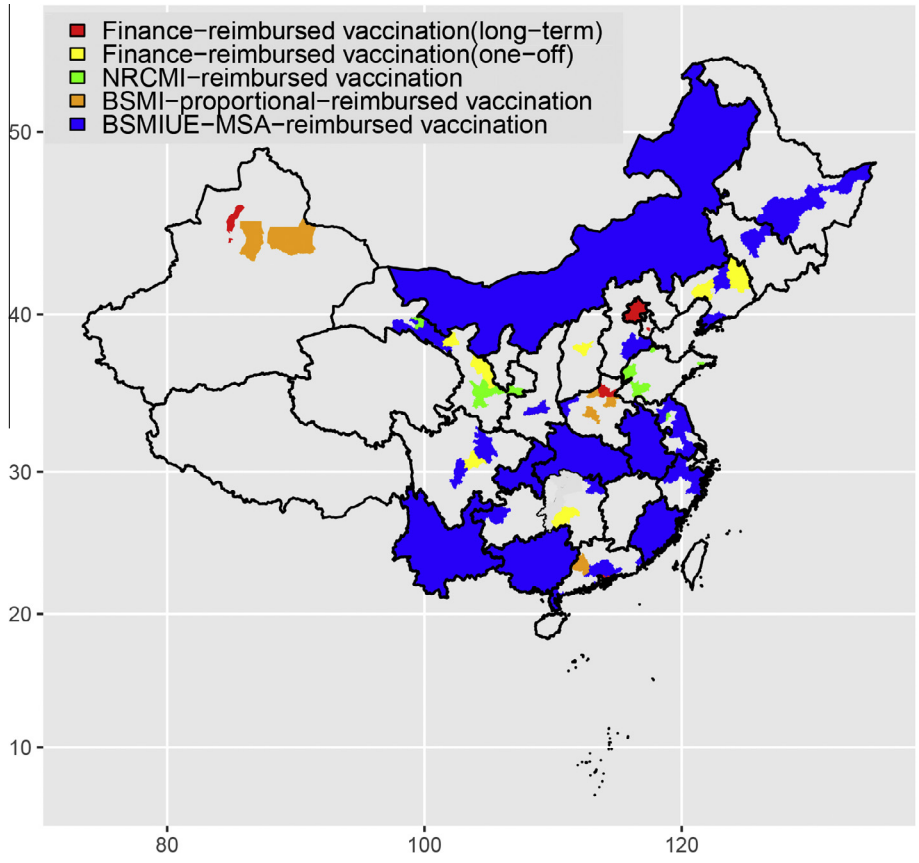

Fig. 1. Map of reimbursement policy for influenza vaccination in China till 2016.

3.1.3. Influenza vaccine coverage

Between 2004 and 2010, influenza vaccine supply increased by 235% from 17·5 to 58·8 million doses. This translates to a rise from 13·6 to 44·1 doses/1000 people, and on average 72·2% of doses were manufactured in China. The sharp increases in dose distribution in the 2010–2011 influenza season were likely because of the greater social attention and public awareness surrounding the 2009 H1N1 pandemic. However, the influence of the pandemic on increased distribution did not last long. After 2010 the number of doses distributed nationally decreased by 35%, to near 2008 levels, with 28·2 doses/1000 people in 2013. This drop was despite 45 of 61 regions beginning reimbursement policies in 2010 or later (Fig. 3). Distributed influenza vaccines were only sufficient for 1·3–3·6% of the total population aged

Table 2
The long-term reimbursement policy for seasonal influenza vaccination in China till 2016.

Province	City/county	Eligible population	Reimbursement fraction of influenza vaccination by government[a]
I. Finance-reimbursed vaccination[b]			
Beijing	/	School children and residents aged 60 years and over	100%
Tianjin	Dongli district	Residents aged 65 years and over	100%
Xinjiang	Karamay	Residents aged 60 years and over, 3–7 years children, school children and teachers, medical workers, polices	100%
Guangdong	Shenzhen	Insured residents aged 60 years old and over	100%
Henan	Xinxiang	Residents aged 65 years and over	100%
II. NRCMI-reimbursed vaccination[b]			
Gansu	(1) Gaotai*, Lingtai*	(1) Insured persons	(1) 80%, 100%
	(2) Min*	(2) Insured persons aged 60 years and over	(2) 100%
Jiangsu	Huaiyin*	Insured persons	30%
Shandong	(1) Liaocheng, Wudi* and Zouping*	(1) Insured persons	(1) US$ 4.84, 100% and 100%, separately
	(2) Wenshang*	(2) Insured persons aged 60 years and over	(2) 100%
III. BSMI-proportional-reimbursed vaccination[b]			
Guangdong	Zhaoqing	Insured persons	30% by BSMIUE and BSMIUR
Henan	Jiaozuo, Kaifeng and Pingdingshan	Insured persons	Separately 40–100%, 100%, and 50–100%
Xinjiang	Changji	Insured persons	100% by BSMIUE
IV. BSMIUE-MSA–reimbursed vaccination[b]			
Anhui, Chongqing, Fujian, Hubei, Guangxi	/	Insured persons	Using the surplus fund of BSMIUE MSA
Inner Mongolia	/	Insured provincial-level employees	Using the surplus fund of BSMIUE MSA
Yunnan	/	Insured persons and their families	Using the surplus fund of BSMIUE MSA
Gansu	Zhangye	Insured persons and their families	Using the surplus fund of BSMIUE MSA
Guangdong	(1) Chaozhou, Dongguan, Foshan, Guangzhou, Huizhou, Zhuhai, Zhanjiang	(1) Insured persons and their families	(1) Using the surplus fund of BSMIUE MSA
	(2) Shenzhen	(2) Insured persons	(2) Using the surplus fund of BSMIUE MSA only when the surplus fund surpass average monthly income in the last year
Guizhou	Bijie	Insured persons	Using the surplus fund of BSMIUE MSA
Hebei	(1) Cangzhou	(1) Insured persons	Using the surplus fund of BSMIUE MSA
	(2) Hengshui	(2) Insured persons and their families	
Heilongjiang	(1) Haerbin	(1) Insured persons	Using the surplus fund of BSMIUE MSA
	(2) Jiamusi	(2) Insured persons and their families	
Henan	Sanmenxia, Xinxiang	Insured persons	Using the surplus fund of BSMIUE MSA
Hunan	Yueyang	Insured persons	Using the surplus fund of BSMIUE MSA
Jiangsu	(1) Lianyungang, Suqian, Suzhou, Wuxi, Yancheng, Yangzhou	(1) Insured persons	Using the surplus fund of BSMIUE MSA
	(2) Taizhou	(2) Insured persons and their families	
Jilin	Changchun	Insured persons	Using the surplus fund of BSMIUE MSA
Liaoning	Dalian, Jinzhou, Panjin, Shenyang	Insured persons	Using the surplus fund of BSMIUE MSA
Shaanxi	Xi'an	Insured persons and their families	Using the surplus fund of BSMIUE MSA
Sichuan	(1) Ya'an	(1) Insured persons	Using the surplus fund of BSMIUE MSA
	(2) Mianyang, Deyang	(2) Insured persons and their families	
Zhejiang	(1) Hangzhou, Ningbo, Shaoxing	(1) Insured persons	Using the surplus fund of BSMIUE MSA
	(2) Huzhou, Taizhou	(2) Insured persons and their families	

/ Province.
* County.
[a] The cost of influenza vaccination is co-paid by individuals and government. The cost that individuals should pay is total cost of influenza vaccination per capita minus the fraction which is reimbursed by government. 100% reimbursement refers to that the vaccinees can get free of charge influenza vaccination at point of care. NRCMI: new rural cooperative medical insurance for rural residents; BSMIUE: basic social medical insurance for urban employees, including Social Pooling Account for inpatient care and individual Medical Savings Account for outpatient care (it represents Social Pooling Account if not specified in this paper); BSMIUR: basic social medical insurance for urban residents; BSMIUE MSA: individual Medical Savings Account of BSMIUE.
[b] Finance-reimbursed vaccination: the cost of influenza vaccination is fully covered by local Financial Department. NRCMI-reimbursed vaccination: the cost of influenza vaccination is proportionally borne by NRCMI. BSMI-proportional-reimbursed vaccination: the cost of influenza vaccination is proportionally paid by BSMIUE and/or BSMIUR. BSMIUE-MSA–reimbursed vaccination: the cost of influenza vaccination is borne using the surplus fund of BSMIUE individual accounts.

6 months and over, and for between 4·5 and 11·5% of the priority populations in China throughout the period. Assuming a manufacture return rate of 31% [10] and a wastage rate of 10% [17], the distributed influenza vaccines was on average sufficient to cover just 1·5% of the total population between 2004 and 2014 (range: 0·8% in 2004 to 2·2% in 2010). Using a manufacture return rate of 14% [10] and a wastage rate of 1% [17], the average uptake rate would be 2·0% (range: 1·1% in 2004 to 3·1% in 2010).

3.2. Budget impact analysis under a free national vaccination program for priority populations

3.2.1. The size of priority population

The population aged six months and over was 1·35 billion in 2013, of which 31.6% (426 million) would be included in the priority populations for influenza vaccination. Of these, 45% (193 million) were the elderly aged 60 years and above, 30% (129 million)

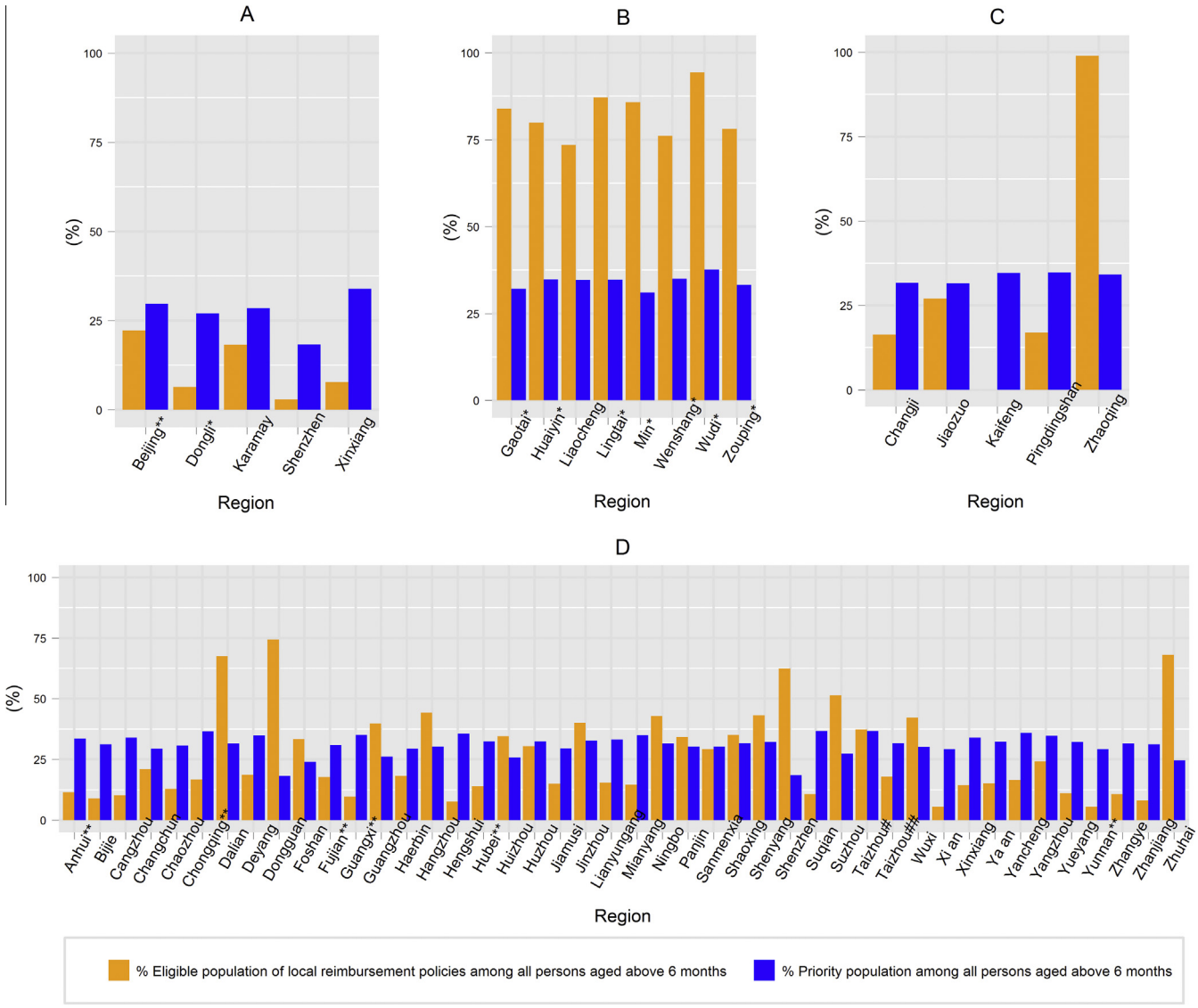

Fig. 2. Proportion of priority populations and eligible subgroup for reimbursed influenza vaccination stratified by policies and by regions. A: The cost of influenza vaccination is fully covered by local Financial Department, called Finance-reimbursed vaccination; B: Proportionately reimbursed by New Rural Cooperative Medical Insurance for rural residents, called NRCMI-reimbursed vaccination; C: Proportionately reimbursed by Basic Social Medical Insurance for urban employees and/or residents, called BSMI-proportional-reimbursed vaccination; D: Paid by surplus fund of Basic Social Medical Insurance for urban employees, called BSMIUE-MSA-reimbursed vaccination. *county; **province; other regions are prefectures. #Taizhou in Jiangsu province; ##Taizhou in Zhejiang province. Note: (1) For six regions (Hubei, Jiamusi, Jilin, Lingtai, Zhangye, and Yancheng) where the reimbursement policy started in 2014, we used the information in 2013 (regarding the number and percentage of priority population and policy covered population) as a proxy due to data availability. (2) In Kaifeng and Inner Mongolia, the proportion of policy covered population was unavailable in 2013. (3) BSMI-proportional-reimbursed vaccination for insured persons in Xi'an of Shaanxi province was only implemented between 2004 and 2006; in 2015, BSMI resumed reimbursement for influenza vaccination, i.e., urban employees can use the surplus fund of individual BSMIUE MSA card to pay for influenza vaccination for their own and their families. Here, we only presented the population of BSMIUE-MSA-reimbursed vaccination policy for Xi'an. (4) We presented here the population of both BSMIUE-MSA–reimbursed vaccination for all insured persons (started from 2008) (panel D) and finance-reimbursed vaccination specifically for insured elderly (started from 2016) (panel A) in Shenzhen, Guangdong province.

were persons aged 5–59 years with underlying chronic illness, 17% (72 million) were children aged 6–59 months, the remaining 8% included pregnant women (22 million), and health-care workers (10 million). The size of the priority populations varied across provinces, ranging from 0·8 million in Tibet province to 32·1 million in Shandong province (Fig. 4A).

3.2.2. Budget impact analysis

Assuming an uptake rate of 20% [42] and a vaccine wastage rate of 10% [17], a free, government-funded national vaccination program for priority populations, would cost the Chinese government US$ 757 (95% CI 726–789) million annually for vaccine purchase and vaccination program operations. Included in this figure is US $ 309 (297–322) million for the elderly, US$ 210 (202–218) million for persons aged 5–59 years with underlying chronic illness, US$ 187 (178–195) million for children aged 6–59 months, US$ 36 (34–37) million for pregnant, and US$ 16 (14–16) million for health-care workers (Table 3). The budget ranged from US$ 1.56 (1.50–1.63) million in Tibet province to US$ 56.73 (54.38–59.08) million in Shandong province (Fig. 4B) (see province details in Table 3). The budget scales proportionally to the vaccine uptake rate. The national budget would be US$ 379 (363–394) million, US$ 1.514 (1.452–1.577) billion and US$ 2·840 (2·722–2·957) billion at an uptake rate of 10%, 40% and 75%, respectively. When

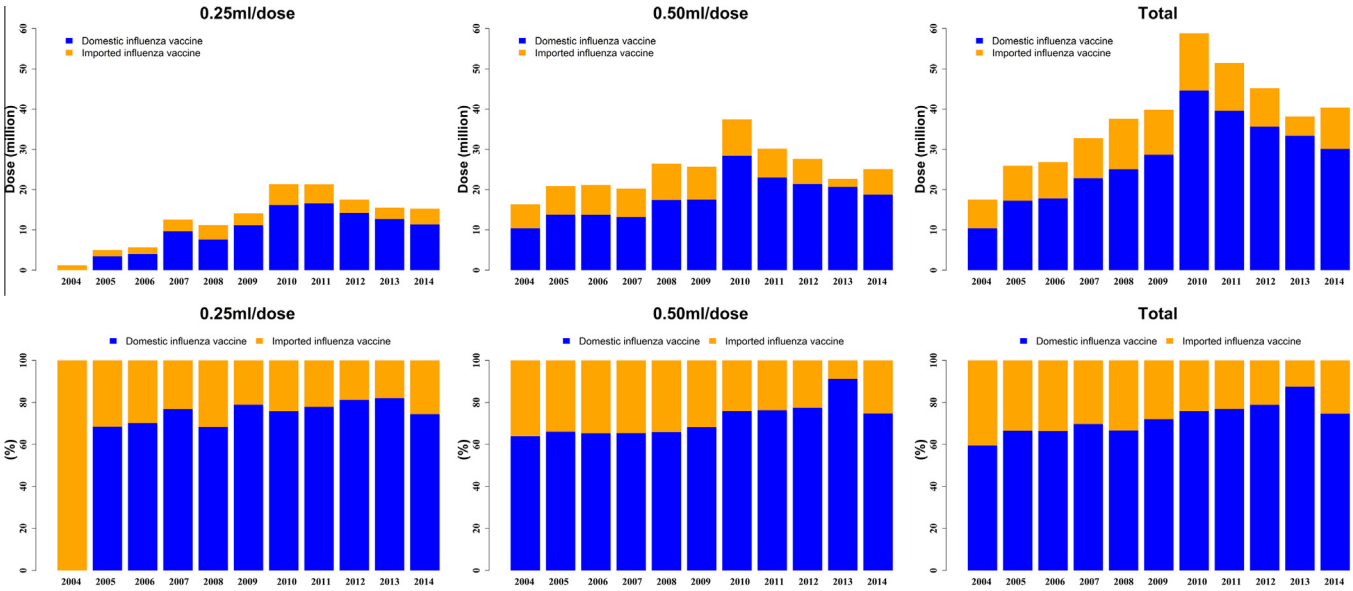

Fig. 3. Numbers and proportion of distributed doses of domestic and imported influenza vaccine in China during 2004–2014.

the wastage rate decreased to 1%, the national budget would be US $ 344 (330–358) million, US$ 688 (660–717) million, US$ 1.377 (1.320–1.434) billion and US$ 2.582 (2.474–2.688) billion at an uptake rate of 10%, 20%, 40% and 75%, separately. When age-specific and risk-group-specific uptake rates were used, the national budget would be US$ 926 (887–965) million and US$ 842 (806–878) billion at a wastage rate of 10% and 1%, respectively.

4. Discussion

The recent vaccine scandal, with massive improperly stored and distributed category 2 vaccines (refers to those used in private sector and paid out of pocket) sold in 24 provinces in China [47], triggered heated debates over the regulation and management of category 2 vaccines. WHO recommends expanding China's category 1 vaccines (refers to those listed in NIP, which are procured and distributed under official arrangement, and provided free of charge) list [15]. The State Council of China released an amended regulation of circulation and management of vaccines. It requires category 2 vaccines to be distributed in the same way as category 1 vaccines [48]. All these may speed up including more category 2 vaccines in NIP.

The seasonal influenza vaccine is one kind of category 2 vaccines, with coverage far below the 2003 WHA targets of at least 75% of the elderly by 2010 [12]. Eliminating or reducing out-of-pocket expenses for vaccination is an important enabling factor for influenza vaccine uptake [13,14,49–52]. To support Chinese government decision makers considering sustainable implementation of a national free influenza vaccination program, we evaluated the current landscape of influenza vaccination across China, and estimated the budget needed for such a program. We found that there was wide variation in seasonal influenza vaccination across provincial-, prefecture- and county-level governments with regards to funding, eligible populations, and reimbursement fractions across these regions.

Existing reimbursement policies were mainly confined to developed regions such as Beijing and Karamay, but were also present in a few less-developed, rural regions. For example, in Min County since 2011, where Gross Regional Product per capita in 2013 (5755 CNY) [53] is only 14% of the national Gross Domestic Product per capita average (GDP: 41,908 CNY) [16], local rural residents aged 60 years old and above who are registered in NRCMI can get influenza vaccination with no out-of-pocket expenses.

In 86% of regions where influenza vaccination was partly or fully paid by BSMI, the policy focused on the insured persons irrespective of medical high-risk status. This mismatch between priority populations and populations eligible for reimbursement creates gaps in coverage and unequal access to vaccination for high risk groups. A national vaccine program ensuring that Immunization of the priority populations would have the largest public health benefit.

Our results suggest that the current reimbursement framework has failed to stimulate demand for influenza vaccination. Two possible reasons may account for this: First, the population eligible for reimbursement (n = 121.5 million) only accounts for about 9% of the national population. Thus, even substantial increases in uptake among groups eligible for reimbursement will have a very small impact on overall national uptake rates. Second, the specific reimbursement policies fail to motivate or incentivize vaccine-seeking behavior. For example, in BSMIUE-MSA-reimbursed vaccination, the individual MSA is an exclusive account only used by the insured persons and sometimes their family members. MSA funds can be used to pay for outpatient and emergency services, as well as some other category 2 vaccines (e.g., Haemophilus Influenza B vaccine) [54]. Hence, the insured individuals typically are less willing to pay for influenza vaccination if they have higher demand for other outpatient medical services and limited funds in their MSA. The precise impact of different payment systems on the uptake of influenza vaccination is important and merits further investigations.

The 2011 dose distribution per 1000 population in China was lower than 88 other countries/regions [55]. Despite a general trend towards increased vaccine supply, the estimated uptake rate has remained low, on average 1·5–2·0% between 2004 and 2014. It was not possible to estimate the age-specific coverage rate in China using lot release data. However, even in Beijing, where free influenza vaccination has been provided to the residents aged 60 years and over since 2007, the coverage rate in the elderly in 2010 was 43·1% [41], which was far below the WHA target, and that in the US (66·7% during the 2014–2015 influenza season) [56], and Brazil (over 70% since 2001) [6]. WHA stated that better use of vaccines for seasonal epidemics will help to ensure that manufacturing

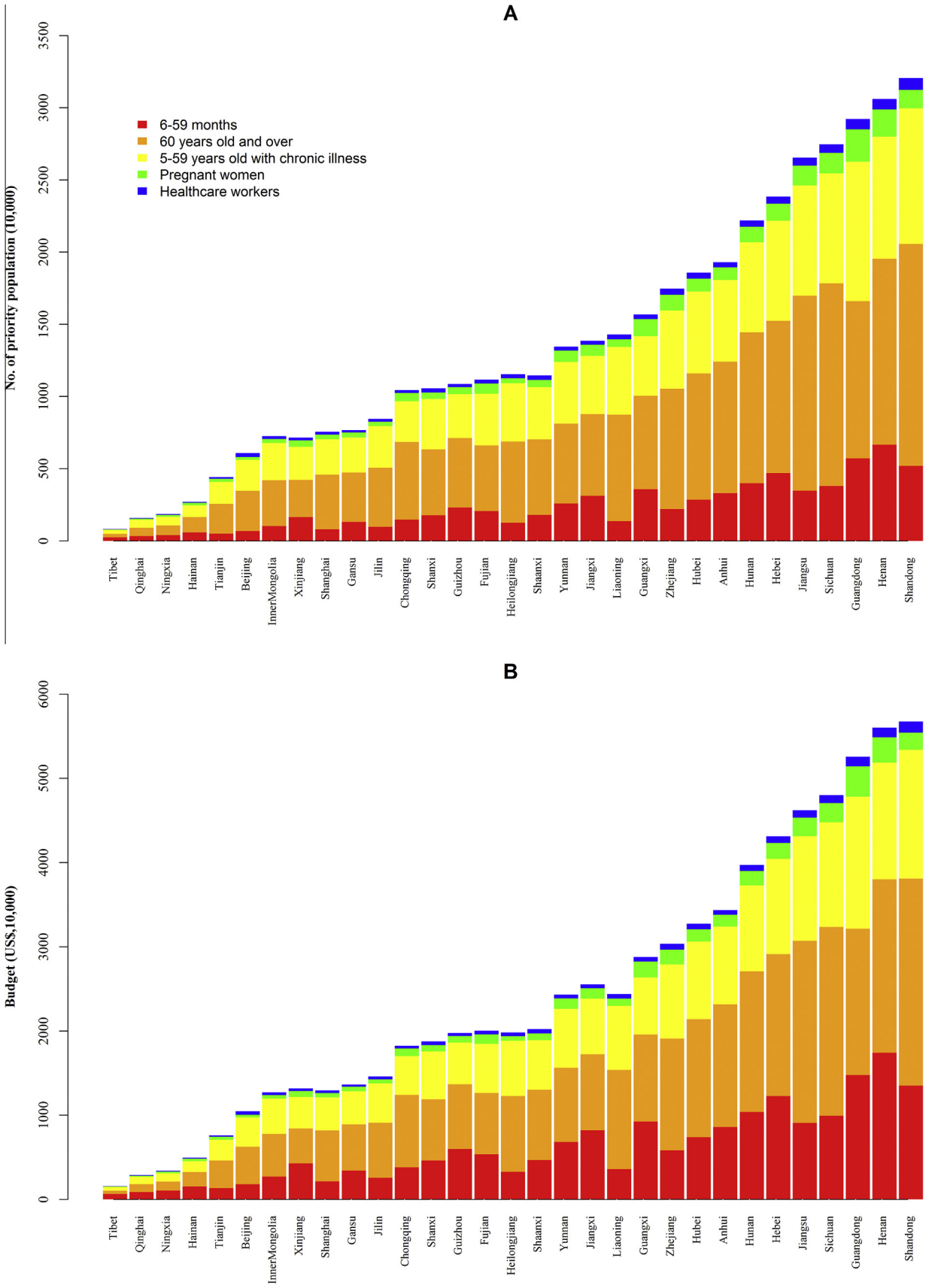

Fig. 4. Number of priority populations and budget for influenza vaccination stratified by provinces, China. A: priority population size. B: Budget under a free national influenza vaccination program for priority population in 2015.

Table 3
Priority populations size stratified by provinces and budget impact analysis under a free national vaccination program.

Region	No. of priority population (thousand)						Budget (million, US$)						Percent of total budget in Government Health Expenditure (‰)[a]	Percent of total budget in Gross Domestic/ Regional Product per capita (‰)[a]
	6–59 months	Elderly	Persons aged 5–59 years with chronic illness	Pregnant	Health workers	Total	6–59 months	Elderly	Persons aged 5–59 years with chronic illness	Pregnant	Health workers	Total		
Beijing	682	2773	2159	199	263	6076	1.80 (1.72–1.88)	4.44 (4.26–4.62)	3.48 (3.34–3.62)	0.32 (0.31–0.33)	0.42 (0.37–0.44)	10.46 (10.03–10.89)	1.767 (1.694–1.839)	0.032 (0.031–0.034)
Tianjin	500	2056	1529	224	107	4415	1.32 (1.26–1.38)	3.29 (3.16–3.42)	2.47 (2.37–2.57)	0.36 (0.34–0.37)	0.17 (0.15–0.18)	7.61 (7.30–7.92)	3.153 (3.023–3.282)	0.032 (0.031–0.033)
Hebei	4699	10,528	6943	1179	492	23,841	12.27 (11.71–12.82)	16.84 (16.17–17.52)	11.31 (10.86–11.77)	1.89 (1.81–1.96)	0.79 (0.69–0.82)	43.10 (41.30–44.89)	6.039 (5.787–6.289)	0.092 (0.088–0.096)
Shanxi	1773	4547	3505	451	284	10,560	4.61 (4.40–4.81)	7.27 (6.98–7.57)	5.69 (5.46–5.92)	0.72 (0.69–0.75)	0.45 (0.40–0.47)	18.75 (17.97–19.53)	4.918 (4.713–5.121)	0.090 (0.086–0.093)
Inner Mongolia	1029	3166	2578	275	196	7244	2.70 (2.58–2.82)	5.07 (4.86–5.27)	4.18 (4.02–4.35)	0.44 (0.42–0.46)	0.31 (0.27–0.33)	12.70 (12.18–13.23)	3.431 (3.289–3.572)	0.045 (0.044–0.047)
Liaoning	1360	7366	4695	539	338	14,298	3.59 (3.43–3.75)	11.79 (11.31–12.26)	7.60 (7.30–7.91)	0.86 (0.83–0.90)	0.54 (0.47–0.56)	24.38 (23.38–25.38)	5.577 (5.348–5.804)	0.054 (0.052–0.056)
Jilin	968	4094	2884	300	200	8446	2.55 (2.43–2.66)	6.55 (6.29–6.81)	4.68 (4.49–4.87)	0.48 (0.46–0.50)	0.32 (0.28–0.33)	14.58 (13.98–15.18)	4.442 (4.259–4.624)	0.068 (0.065–0.070)
Heilongjiang	1249	5627	4030	348	279	11,533	3.27 (3.12–3.42)	9.00 (8.64–9.37)	6.54 (6.28–6.81)	0.56 (0.53–0.58)	0.45 (0.39–0.46)	19.82 (19.01–20.63)	5.779 (5.541–6.015)	0.083 (0.080–0.086)
Shanghai	809	3778	2441	324	192	7544	2.13 (2.03–2.22)	6.04 (5.80–6.29)	3.94 (3.78–4.10)	0.52 (0.50–0.54)	0.31 (0.27–0.32)	12.94 (12.41–13.47)	3.106 (2.979–3.233)	0.036 (0.035–0.038)
Jiangsu	3471	13,510	7631	1379	551	26,542	9.08 (8.67–9.48)	21.62 (20.75–22.49)	12.42 (11.92–12.92)	2.21 (2.12–2.30)	0.88 (0.77–0.92)	46.20 (44.29–48.10)	5.066 (4.857–5.274)	0.047 (0.045–0.049)
Zhejiang	2211	8313	5422	1095	427	17,468	5.80 (5.54–6.06)	13.30 (12.76–13.84)	8.80 (8.44–9.15)	1.75 (1.68–1.82)	0.68 (0.60–0.71)	30.34 (29.09–31.58)	4.647 (4.455–4.837)	0.049 (0.047–0.051)
Anhui	3303	9099	5665	876	354	19,297	8.60 (8.21–8.98)	14.56 (13.97–15.14)	9.24 (8.86–9.61)	1.40 (1.35–1.46)	0.57 (0.49–0.59)	34.36 (32.93–35.78)	4.981 (4.774–5.187)	0.109 (0.104–0.113)
Fujian	2057	4543	3593	709	262	11,164	5.35 (5.10–5.59)	7.27 (6.98–7.56)	5.85 (5.62–6.09)	1.13 (1.09–1.18)	0.42 (0.37–0.44)	20.02 (19.19–20.85)	4.499 (4.311–4.685)	0.055 (0.053–0.058)
Jiangxi	3128	5645	4037	778	270	13,857	8.19 (7.82–8.56)	9.03 (8.67–9.40)	6.61 (6.34–6.88)	1.24 (1.19–1.29)	0.43 (0.38–0.45)	25.51 (24.44–26.57)	4.716 (4.518–4.912)	0.107 (0.103–0.112)
Shandong	5195	15,369	9398	1271	819	32,053	13.51 (12.89–14.11)	24.59 (23.60–25.58)	15.29 (14.67–15.91)	2.03 (1.95–2.12)	1.31 (1.14–1.36)	56.73 (54.38–59.08)	5.979 (5.730–6.225)	0.062 (0.060–0.065)
Henan	6662	12,873	8467	1885	716	30,604	17.42 (16.63–18.19)	20.60 (19.77–21.43)	13.84 (13.28–14.40)	3.02 (2.89–3.14)	1.15 (1.00–1.19)	56.01 (53.67–58.34)	6.009 (5.758–6.259)	0.105 (0.101–0.109)
Hubei	2841	8751	5674	902	411	18,579	7.38 (7.04–7.71)	14.00 (13.44–14.57)	9.24 (8.87–9.61)	1.44 (1.39–1.50)	0.66 (0.57–0.68)	32.72 (31.37–34.07)	5.350 (5.128–5.570)	0.080 (0.077–0.083)
Hunan	3991	10,439	6261	1062	442	22,196	10.37 (9.90–10.83)	16.70 (16.03–17.38)	10.22 (9.81–10.63)	1.70 (1.63–1.77)	0.71 (0.62–0.74)	39.70 (38.04–41.34)	6.084 (5.831–6.336)	0.098 (0.094–0.102)
Guangdong	5723	10,871	9668	2248	708	29,219	14.76 (14.09–15.42)	17.39 (16.69–18.09)	15.67 (15.04–16.30)	3.60 (3.45–3.74)	1.13 (0.99–1.18)	52.56 (50.36–54.74)	4.740 (4.542–4.937)	0.051 (0.049–0.053)
Guangxi	3574	6461	4145	1174	335	15,688	9.24 (8.81–9.65)	10.34 (9.92–10.75)	6.78 (6.51–7.05)	1.88 (1.80–1.95)	0.54 (0.47–0.56)	28.77 (27.56–29.97)	5.372 (5.146–5.596)	0.120 (0.115–0.126)
Hainan	580	1065	811	183	63	2702	1.52 (1.45–1.59)	1.70 (1.64–1.77)	1.32 (1.27–1.38)	0.29 (0.28–0.30)	0.10 (0.09–0.11)	4.94 (4.73–5.14)	3.842 (3.681–4.001)	0.095 (0.091–0.098)
Chongqing	1465	5379	2825	571	198	10,438	3.81 (3.63–3.97)	8.61 (8.26–8.95)	4.59 (4.41–4.78)	0.91 (0.88–0.95)	0.32 (0.28–0.33)	18.24 (17.48–18.99)	4.842 (4.642–5.042)	0.087 (0.083–0.090)
Sichuan	3808	14,016	7632	1415	596	27,467	9.93 (9.47–10.37)	22.43 (21.52–23.33)	12.43 (11.93–12.93)	2.26 (2.17–2.36)	0.95 (0.83–0.99)	48.00 (46.02–49.98)	5.293 (5.074–5.511)	0.110 (0.106–0.115)
Guizhou	2314	4796	3045	483	222	10,860	5.98 (5.70–6.24)	7.67 (7.37–7.98)	4.97 (4.77–5.17)	0.77 (0.74–0.80)	0.35 (0.31–0.37)	19.75 (18.92–20.57)	4.277 (4.098–4.455)	0.149 (0.142–0.155)
Yunnan	2596	5506	4295	786	266	13,449	6.81 (6.50–7.11)	8.81 (8.45–9.16)	7.00 (6.72–7.28)	1.26 (1.21–1.31)	0.42 (0.37–0.44)	24.30 (23.28–25.30)	4.542 (4.353–4.730)	0.125 (0.120–0.130)

Table 3 (*continued*)

Region	No. of priority population (thousand)						Budget (million, US$)						Percent of total budget in Government Health Expenditure (‰)[a]	Percent of total budget in Gross Domestic/Regional Product per capita (‰)[a]
	6–59 months	Elderly	Persons aged 5–59 years with chronic illness	Pregnant	Health workers	Total	6–59 months	Elderly	Persons aged 5–59 years with chronic illness	Pregnant	Health workers	Total		
Tibet	235	251	264	43	25	819	0.62 (0.59–0.65)	0.40 (0.39–0.42)	0.43 (0.42–0.45)	0.07 (0.07–0.07)	0.04 (0.03–0.04)	1.56 (1.50–1.63)	1.978 (1.895–2.061)	0.117 (0.112–0.121)
Shaanxi	1807	5207	3630	493	322	11,458	4.67 (4.46–4.88)	8.33 (8.00–8.67)	5.90 (5.66–6.14)	0.79 (0.76–0.82)	0.52 (0.45–0.54)	20.21 (19.37–21.04)	4.139 (3.967–4.310)	0.076 (0.073–0.079)
Gansu	1319	3420	2419	347	161	7666	3.41 (3.26–3.56)	5.47 (5.25–5.69)	3.94 (3.78–4.10)	0.56 (0.53–0.58)	0.26 (0.22–0.27)	13.63 (13.07–14.20)	4.363 (4.182–4.544)	0.131 (0.126–0.136)
Qinghai	327	586	536	85	45	1579	0.86 (0.82–0.90)	0.94 (0.90–0.98)	0.87 (0.84–0.91)	0.14 (0.13–0.14)	0.07 (0.06–0.07)	2.88 (2.76–3.00)	2.220 (2.127–2.312)	0.083 (0.079–0.086)
Ningxia	398	668	599	134	48	1847	1.04 (1.00–1.09)	1.07 (1.03–1.11)	0.98 (0.94–1.02)	0.21 (0.21–0.22)	0.08 (0.07–0.08)	3.38 (3.24–3.52)	3.369 (3.228–3.509)	0.079 (0.076–0.083)
Xinjiang	1634	2594	2279	451	190	7149	4.27 (4.07–4.46)	4.15 (3.98–4.32)	3.72 (3.57–3.87)	0.72 (0.69–0.75)	0.30 (0.26–0.32)	13.16 (12.61–13.71)	3.799 (3.639–3.957)	0.095 (0.091–0.099)
Total	71,710	193,300	129,061	22,210	9780	426,061	187 (178–195)	309 (297–322)	210 (202–218)	36 (34–37)	16 (14–16)	757 (726–789)	4.777 (4.579–4.975)	0.080 (0.077–0.083)

[a] Government Health Expenditure and Gross Domestic/Regional Product per capita in 2013 was separately obtained from China health statistics yearbook 2015 and China Statistical Yearbook 2014, then inflated to 2015 CNY using consumer price index and expressed in US dollars using the median 2015 exchange rate of 1 US$ = 6·2 CNY.

capacity meets demand in a future pandemic [12]. This low coverage precluded any meaningful control of seasonal disease burden and negatively impacted China's preparedness for an influenza pandemic. To improve seasonal influenza vaccine coverage, reduce the disease burden and prepare for the next pandemic in China, will require political commitment and sustained public health investment.

We evaluated the budget needed to fund a potential national program on influenza vaccination. This money (US$ 757 million, 95%CI 726–789) is 4.777‰ (4.579–4.975) of total government health expenditures and 0·080‰ (0.077–0.083) of GDP in 2015. To quantify and compare such a program with other health-care decisions, it would be helpful to implement a cost-effectiveness analysis that incorporates the annual outlay due to vaccine costs (calculated in this study) as well as (1) the downstream cost savings through averted medical visits and deaths, and (2) the quality of life gained through decreased influenza-associated morbidity and mortality.

This was the first study to comprehensively collect influenza vaccine reimbursement information across China. Our online survey was conducted at the provincial-level CDCs because of the difficulty of contacting all district-level CDCs, a few of whom could not provide complete information for their entire province. Although we supplemented the survey data with information obtained from official websites, there was some missing information. In spite of this limitation, we believe this study provides a detailed picture of the current reimbursement policy landscape. Our budget analysis may underestimate total costs as we did not assess the need for additional investments in the vaccine cold chain that could be required to support a national influenza vaccination program.

5. Conclusions

This was the first detailed analysis of the landscape of influenza vaccine reimbursement policies across China. Although an increasing number of regional governments have begun to pay, partially or fully, for influenza vaccination for selected groups, this patchwork of small-scale sub-national policies have failed to increase national uptake of the vaccine, which remains low. A national, free seasonal influenza vaccination program for priority populations would be costly; a cost-effectiveness analysis is needed to identify the most efficient way to improve vaccination coverage rates and better control influenza disease burden in China.

Contributors

JY, LF and HY designed the analysis; JY, LF, MP, YZ and XL collected data; JY, KA conducted the data analysis and drafted the manuscript; JY, KA, LF, BC and HY contributed to the interpretation of the results and to the revision of the manuscript.

Conflict of interest

None.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.vaccine.2016.10.013.

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